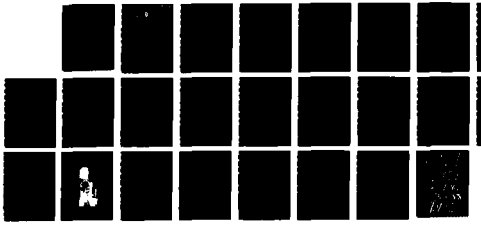
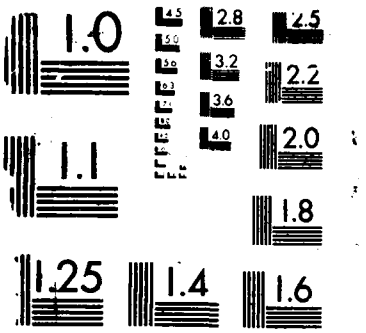
AD-A188 358 ACUTE MOUNTAIN SICKNESS AT 4500 M IS NOT ALTERED BY REPEATED EIGHT-HOUR E (U) ARMY RESEARCH INST OF ENVIRONMENTAL MEDICINE NATICK MA R L BURSE ET AL 1/1

UNCLASSIFIED 10 SEP 87 F/G 6/10 NL





MICROCOPY RESOLUTION TEST CHART

UNCLASSIFIED
SECURITY CLASSIFICATION OF THIS PAGE

DTIC FILE COPY

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED	1b. RESTRICTIVE MARKINGS NONE
AD-A188 358 DTIC ELECTE NOV 20 1987 D	3. DISTRIBUTION/AVAILABILITY OF REPORT Approved for public release; distribution is unlimited.
4. PERFORMING ORGANIZATION REPORT NUMBER(S)	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION USARIEM 6b. OFFICE SYMBOL (If applicable) SGRE-UE-AR	7a. NAME OF MONITORING ORGANIZATION
6c. ADDRESS (City, State, and ZIP Code) Natick, MA 01760-5007	7b. ADDRESS (City, State, and ZIP Code)
8a. NAME OF FUNDING/SPONSORING ORGANIZATION 8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
8c. ADDRESS (City, State, and ZIP Code)	10. SOURCE OF FUNDING NUMBERS PROGRAM ELEMENT NO. / PROJECT NO. 3E162777 A879 / TASK NO. 879/BD / WORK UNIT ACCESSION NO.

11. TITLE (Include Security Classification)
Acute Mountain Sickness at 4500 m Is Not Altered by Repeated Eight-Hour Exposures to 3200-3550 m Normobaric Hypoxic Equivalent (Unclas.)

12. PERSONAL AUTHOR(S)
RICHARD L. BURSE, Sc.D., and VINCENT A. FORTE, Jr., M.A.T.

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
Journal Article	FROM _____ TO _____	87-09-10	27

16. SUPPLEMENTARY NOTATION

17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	altitude acclimation, rebreathing device, hypoxic stimulus, ventilatory and hematological responses.

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

A lightweight device, designed to supply inspired air at 12.8% O_2 concentration (PO_2 equivalent to 3900 m altitude) by recirculating a portion of each expired breath after CO_2 removal, was tested at sea-level for its ability to induce altitude acclimation. Twelve young men (experimental group) breathed from the device for 7.5-8 h each day for ten successive days. On the morning of day 1, inspired O_2 concentrations averaged 12.8%, as intended, but increased by noontime and remained elevated thereafter. This raised the average hypoxic stimulus to 13.8 ± 0.9% (PO_2 equivalent to 3370 ± 517 m altitude) for the entire ten-day period. Ten other young men (control group) breathed normoxic air from a placebo device of identical appearance on the same schedule. On the tenth day, both groups were exposed for two days to 4500 m altitude in a hypobaric chamber to assess the effect of the treatment on acute mountain sickness (AMS). After the sea-level treatment, the experimental group showed no significant differences from control in resting ventilatory rate, respiratory frequency or end-tidal PO_2, but end-tidal PCO_2 was lower; there was no indication of hemoconcentration

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION
☒ UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT ☐ DTIC USERS	UNCLASSIFIED

22a. NAME OF RESPONSIBLE INDIVIDUAL	22b TELEPHONE (Include Area Code)	22c. OFFICE SYMBOL
RICHARD L. BURSE, Sc.D.	(617) 651-4893	SGRD-UE-AR

DD Form 1473, JUN 86 Previous editions are obsolete.

SECURITY CLASSIFICATION OF THIS PAGE
UNCLASSIFIED

A

87 10 28 20

Block 19 (continued):

At altitude, both groups showed the expected decreases in end-tidal PO_2 and PCO_2, and increases in hemoglobin concentration and hematocrit indicative of hemoconcentration, with no differences between them. Neither incidence nor severity of AMS differed significantly between groups, but the experimental group had a lower incidence rate than historical control The cause of the decrease in the sea-level treatment stimulus from 3900 to 3370 m could not be determined from the experimental data. It was clear, however, that administering such a stimulus for 8 h each day, even for ten successive days, was not sufficient to induce any meaningful degree of acclimation to 4500 m or to induce any beneficial ventilatory or hematological responses to that altitude.

ACUTE MOUNTAIN SICKNESS AT 4500 m IS NOT ALTERED BY REPEATED EIGHT-HOUR EXPOSURES TO 3200-3550 m NORMOBARIC HYPOXIC EQUIVALENT

Richard L. Burse, Sc.D.
and
Vincent A. Forte, Jr., M.A.T.

Altitude Research Division
U.S. Research Institute of Environmental Medicine
Natick, Massachusetts 01760-5007

Running Head: Eight-hour hypoxic exposures and mountain sickness

Address correspondence to:

Dr. Richard L. Burse
Altitude Research Division
U.S. Army Research Institute of
Environmental Medicine
Natick, Massachusetts 01760-5007
(617) 651-4893

ABSTRACT

A lightweight device, designed to supply inspired air at 12.8% O_2 concentration (PO_2 equivalent to 3900 m altitude) by recirculating a portion of each expired breath after CO_2 removal, was tested at sea-level for its ability to induce altitude acclimation. Twelve young men (experimental group) breathed from the device for 7.5-8 h each day for 10 successive days. On the morning of day 1, inspired O_2 concentrations averaged 12.8%, as intended, but increased by noontime and remained elevated thereafter. This raised the average hypoxic stimulus to 13.8 ± 0.9 % (PO_2 equivalent to 3370 $\pm$ 517 m altitude) for the entire 10-day period. Ten other young men (control group) breathed normoxic air from a placebo device of identical appearance on the same schedule. On the tenth day, both groups were exposed for 2 days to 4500 m altitude in a hypobaric chamber to assess the effect of the treatment on acute mountain sickness (AMS). After the sea level treatment, the experimental group showed no significant differences from control in resting ventilatory rate, respiratory frequency or end tidal PO_2, but end-tidal PCO_2 was lower; there was no indication of hemoconcentration. At altitude, both groups showed the expected decreases in end-tidal PO_2 and PCO_2, and increases in hemoglobin concentration and hematocrit indicative of hemoconcentration, with no differences between them. Neither incidence nor severity of AMS differed significantly between groups, but the experimental group had a lower incidence rate than historical controls. The cause of the decrease in the sea-level treatment stimulus from 3900 to 3370 m could not be determined from the experimental data. It was clear, however, that administering such a stimulus for 8 h each day, even for 10 successive days, was not sufficient to induce any

meaningful degree of acclimation to 4500 m or to induce any beneficial ventilatory or hematological responses to that altitude.

Index Terms: altitude acclimation, rebreathing device, hypoxic stimulus, ventilatory and hematological responses.

INTRODUCTION

Acute mountain sickness (AMS) is a debilitating and occasionally fulminating illness experienced within 1-4 days by individuals ascending directly to altitudes above 3000 m. Symptoms of AMS, although not unique to that disorder, form a definable constellation including: headache, nausea, with or without vomiting, loss of appetite, sleeplessness, breathlessness and dizziness at rest, irritability, lassitude and general malaise (3,9,13). Symptoms usually develop within the first 4 days, either right after initial ascent to high altitude or upon subsequent ascent to a higher one, and usually resolve spontaneously within a few days to a week. Incidence rates and severity of AMS appear to be a function of both elevation and rapidity of ascent (10,13). Because uncomplicated AMS can be severe enough to disable its sufferer and complicated AMS can progress to the potentially fatal pulmonary and cerebral edemas of high altitude (10), prevention or palliation of the incapacitating symptoms is desirable (9). At present, the most effective method to prevent or limit AMS symptomatology is staging (2-4 day residences after every 500-1000 m of elevation increase, beginning at 2500 m)(9). This technique allows the body to partially acclimate to each successive altitude, but requires adequate time, transportation, and staging sites at the appropriate elevations. Adjuvenant drug therapy is also useful: acetazolamide, 500-1000 mg/day, for 2 days before and 2 days after ascent, reduces symptom severity (8) but works best when combined with staging (7). Dexamethasone (4 mg q.i.d., same schedule) is also of marked benefit, albeit not without potential complications (14,18). It is obvious, therefore, that a regimen easily administered at sea level which could mimic the acclimating effects of

staging would be very useful to high altitude sojourners, used either by itself or with adjuvenant drug therapy.

Recently, clever devices have been developed for physical conditioning which reduce the O_2 content of inspired air below ambient levels (21). Such a device appeared to offer some potential for providing a hypoxic stimulus for acclimation. Accordingly, one such device was modified by its originator (Inspir Air Corp, Westlake, CA) to provide inspired air of an O_2 concentration equivalent to 3970 ± 300 m altitude. This device was then tested to determine if using it 7-8 h per day for 10 consecutive days would reduce the severity of AMS during a subsequent 48-h challenge test in an altitude chamber at 4500 m.

MATERIALS AND METHODS

Simulator Functioning: The 4.3 kg altitude simulator, shown in Figure 1, was worn on the back by means of pack-straps. Inspired air was provided to an oronasal anaesthesia mask at sub-ambient O_2 tensions by the technique of partial recirculation of the low- O_2 expired air. Recirculation was accomplished by channelling expired air from the mask through a 19 mm ID flexible tube with a one-way check valve and past an orifice of fixed size which vented only part of each exhaled breath to the atmosphere. The remainder of each exhaled breath entered a mixing chamber where, during the next inspiration, ambient air was drawn in through the orifice and mixed with the expired air by a swirling action imparted by static vanes in the chamber. The resultant low O_2 mixture of expired and ambient air was then drawn through two

CO_2 scrubbing canisters in series (Baralyme, Allied Healthcare Products, St. Louis, MO) and into the 19 mm inspired air hose leading to the face mask. Preliminary tests at sea level showed that O_2 tension was a function principally of orifice diameter and, to a slight extent, of ventilatory rate as oxygen consumption (VO_2) was increased. During the tests, four pilot subjects performed repeated bouts of cycle exercise at intensities ranging from sitting quietly to moderate exercise (VO_2 from 0.7 to 2.2 $L \cdot min^{-1}$). These tests were used by the simulator's developer to set the orifice at a fixed size that produced a mean value of inspired O_2 of 12.8% (3960 m altitude equivalent) during seated rest. The mean O_2 value was found to increase to no more than 13.0% (3750 m) at the maximum VO_2 tolerated by each pilot subject. The upper tolerance limit was found to lie between 1.8 and 2.2 $L \cdot min^{-1}$ and was determined by the inspired air becoming unacceptably warm due to the exothermic CO_2 scrubbing reaction. Subjects were required, therefore, to limit their physical activity to a moderate walking pace (VO_2 = 1.2-1.8 $L \cdot min^{-1}$) and to slow down if the inspired air became uncomfortably warm. It was also determined in these pilot tests that no CO_2 breakthrough occurred, even after the scrubber had been used for 8 hours.

A placebo simulator, used by the control subjects, was the same breathing device altered to vent all expired air through the main orifice and draw in all inspired air through a separate, concealed orifice leading to the inspired air hose. Scrubbing canisters were changed daily for both the actual and placebo devices. Each subject had his own numbered device, which was disassembled, washed and disinfected (benzalkonium chloride, 1:1000 v/v) each evening.

Subjects: Male soldiers, 18 to 26 years old, were recruited for this study from two low-altitude locations within the United States. They voluntarily signed statements of informed consent after receiving detailed explanations of the procedures and risks involved. Subject numbers were randomly assigned to the experimental and control groups by lot; the experimental group comprised 12 men, while the control group comprised 10.

Sea level phase: The acclimating regimen was structured to be as realistic as possible, consonant with subjecting the simulators to a fair test of their ability to induce partial acclimation. To this end, ten consecutive days were selected as the longest period any climbing group was likely to use the simulator, just prior to their ascent. Similarly, eight h per day appeared to be the maximum duration of use, which would still leave time for other activities mandated by the forthcoming ascent but incompatible with simulator use (physical training, hauling of equipment, loading of transport, face-to-face communication, etc.). Fixed breaks were incorporated in the daily schedule for activities requiring removal of the face mask (liquid intake, communication with others, and the noon meal).

Subjects donned the simulators no sooner than 1/2 h after breakfast. Inspired O_2 and CO_2 concentrations were immediately checked with a mass spectrometer (Perkin-Elmer Model 1100A). The device was then used for about 4 h (until lunch break), with a 15-min break after 2 h. After lunch, subjects used the device for 4 h in the afternoon, with another 15 min-break halfway. O_2 and CO_2 concentrations were also checked at the start and end of the afternoon. To elevate metabolic and ventilatory rate above resting levels and also relieve boredom, all subjects walked outdoors in a group on mostly level

terrain for 90 min each morning and afternoon. Activity levels were sedentary, otherwise: 90 minutes was spent each morning training for cognitive pencil and paper tasks to be performed at altitude and the rest of the day was spent reading, writing, or watching TV.

Altitude Phase: All subjects began two days of exposure in a hypobaric chamber at 4500 m simulated altitude on the afternoon or evening of the tenth treatment day. During the exposure, AMS symptomatology was assessed each morning and evening. Subjects performed a battery of cognitive performance tasks for 90 minutes each morning (to be reported elsewhere) and had their ventilatory function assessed each afternoon, as had been done before and after the sea level treatment period. The remainder of the time was spent watching TV, reading, card playing, or sleeping. Exposures were terminated on the afternoon of the second day as soon as all ventilatory function tests were complete.

Measurements: Respiratory parameters potentially indicative of the development of ventilatory acclimation to hypoxia were measured before and after treatment at sea level and on both days at altitude. Resting ventilatory rate (V_E) was measured for 3 min after 5 min quiet sitting, by means of a direct-reading turbine spirometer (KL Engineering Inc., Model S300-C) previously calibrated by Tissot spirometry. End-tidal values for PO_2 and PCO_2 were obtained from continuous air samples at the mouthpiece during measurement of ventilatory rate, analyzed by mass spectrometry (Perkin-Elmer Corp., Model 1100A). Spectrometer output was recorded (Gould Instruments, Inc., Model 2200) and averaged over a 3 min period; respiration rate (RR) was counted from these records and similarly averaged.

To determine the effect of simulator use and altitude exposure on hemoglobin concentrations and hematocrit ratios, these parameters were also measured before and after the sea-level treatment period and on each morning at altitude. Blood, red cell and plasma volumes were calculated from hemoglobin concentration and hematocrit by the method of Dill and Costill (5).

AMS was assessed each morning and evening at altitude in two ways. The first was to ask each subject whether or not he felt sick and, if so, to what degree: slight, moderate or severe. The second was to collect each subject's responses to the 67-item Environmental Symptoms Questionnaire (ESQ, 20) and weight them according to the method of Sampson et al. (19) for the calculation of scores for the cerebral and respiratory forms of AMS (AMS-C and AMS-R, respectively). By this method, AMS-C scores greater than 0.70 and AMS scores greater than 0.60 are considered to indicate illness. Both the global question and ESQ methods of assessing illness were utilized in order to maximize the possibility of detecting any advantage to the experimental group.

Study design and analysis: The experiment was of single-blind design; only the experimenters knew which individuals were assigned to the experimental and placebo devices. Comparisons between the experimental and control groups in their ventilatory and hematological parameters were made by independent t-test. Pre-post treatment and altitude comparisons within each group were made by one-way, repeated measures analyses of variance, followed by Tukey HSD post-hoc tests, if warranted. Significance of differences in incidence of AMS at altitude between the experimental and control groups was determined by chi-square testing, using Yates' correction. The level of significance for all tests was arbitrarily chosen as $P < 0.05$.

RESULTS

Sea-level preliminary phase: Due to scheduled breaks and unavoidable delays, the actual daily use of the altitude simulators was slightly less than the planned eight hours. The average period of use, for all subjects combined, was 7.65 h for days 1-9, 7.8 h on day 10 for 8 subjects and 3.9 h on day 10 for the remaining 14 subjects. The latter subjects were sent to altitude after lunch on day 10, rather than after supper, to increase their chances of developing significant AMS symptoms by morning.

The average altitude equivalents for the experimental group over the 10-day sea level treatment period, determined from the ICAO conversion tables (15), are shown in Table 1. The initial readings on the morning of day 1 averaged 3944 ± 460 m, very close to the design value of 3962 ± 305 m. This design value was not maintained by the simulator, however. The average dropped to 3295 m by noon and held generally within the range of 3200-3550 m thereafter for the remainder of the treatment period. The average stimulus for acclimation over the entire 10-day period was 3370 ± 517 m, lower than was intended by 600 m. There was no discernable pattern to the fluctuations throughout the 10-day period after the reduction in altitude equivalent which occurred during day 1, either in the group mean values (shown) or the individual measurements (not shown).

Table 1

The resting ventilatory parameters, measured at sea level before and immediately after the period of simulator use, are shown in Table 2 for the control and experimental groups. As expected, the control group showed no significant changes in minute ventilation, respiratory rate or end-tidal PO_2 and PCO_2. The experimental group showed an 11% decrease ($P < 0.05$) in its mean end-tidal PCO_2 from 38 to 34 torr, however. This was accompanied by a 15% decrease in respiratory frequency and a 13% increase in minute ventilation. Although the change in minute ventilation was not significant, the change in respiratory frequency was ($P < 0.05$); the resulting 35% increase in calculated tidal volume was significant and was consistent with the significantly enhanced wash-out of alveolar CO_2.

Table 2

Altitude phase: Table 2 also shows the resting ventilatory measurements at altitude. Both the experimental and control groups exhibited the expected immediate hyperventilatory response to the hypoxia, leading to significantly depressed end-tidal PCO_2 values throughout the exposure. The groups differed only in their end-tidal PCO_2 values, however, with the experimental group having the lower values. This was consistent with their lower values throughout the sea level treatment period. The experimental group had no obvious advantage at altitude in either minute ventilatory rate or alveolar oxygenation as a result of their prior hypoxic exposure during the sea-level treatment period.

The AMS experience at altitude also showed the experimental group to have no advantage. The responses to the questions, "Do you feel sick?" and "If so, how sick?" are shown in Table 3. Seventy percent of the control group and fifty percent of the experimental group reported some degree of feeling sick, nowhere near being different ($\chi^2 = 0.26$, d.f. = 1, $0.5 < P < 0.9$). When the degree of reported sickness was weighted on a 4-point scale (none = 0, very sick = 3), the mean scores for those in the experimental and control groups who got sick differed by less than one standard error ($t = 0.47$, $0.4 < P < 0.7$), indicating almost identical sickness severity.

Table 3

These global reports of feeling sick were supported by calculations of AMS-C and AMS-R scores from the severity of each individual's symptoms reported morning and evening on the ESQ. The most severe AMS-C and AMS-R scores for each individual, irrespective of when they occurred during the altitude exposure, were selected to indicate the presence or absence of AMS during the exposure. Means were calculated from these individual peak scores for the experimental and control groups as a whole and then for the sub-set of each group that met the criteria for having AMS-C and AMS-R. These means are shown in Table 4. The experimental group did not differ significantly from the control group in the mean scores for AMS-C or AMS-R, either as a whole or for the sub-set manifesting illness. The incidence of AMS-C in the control group

was 100%, which contradicted the responses of 30% of that group who reported not feeling sick when asked directly. The experimental group, however, reported similar incidence rates of AMS-C and for feeling sick. The difference between the two groups in the incidence of AMS-C approached, but did not reach, significance ($0.05 < P < 0.1$). For AMS-R, the incidence was 50% in the experimental group and 80% in the control group (not different); these were very similar to the responses to the global question.

Table 4

The hemoglobin concentrations and hematocrit ratios before and after the sea-level treatment period and on the two days at altitude are shown in Table 5. Also shown are the calculated percentage changes in the red cell and plasma components of total blood volume. There was a significant reduction in hemoglobin concentration in the control group over the sea level treatment period, with a concomitant, but non-significant, decrease in hematocrit. There was an 11% increase in plasma volume ($P < 0.05$), and a 7% increase in RCV (NS), resulting in a 9% increase in blood volume. The experimental group showed indications of hemodilution also, but none of the measured or calculated changes reached significance. Upon exposure to altitude, however, both groups hemoconcentrated as expected. On the first day, the changes in total blood volume, and the component red cell and plasma volumes, were nearly identical in both groups. On the second day, the experimental group showed the greater

plasma volume loss, but none of the differences between groups were significant.

Table 5

DISCUSSION

The altitude simulators were used an average of 7.42 h each day, about 1/2 h less than scheduled. This was unlikely to have markedly influenced the results. On days 1-9, only 20 min were lost on average, by extending the scheduled breaks to accomplish necessary face-to-face and telephonic communications which were prevented by the face mask. The remaining time was lost on day 10 during post-treatment measurement of resting ventilation and by those subjects sent to altitude after lunch rather than after supper. It is possible, however, that the return to normoxia every 2 h during the scheduled breaks may have inhibited the acclimation process. Continuous hypoxic exposure for 7.5-8 h might well have produced a different result, but the logistical requirements for food and liquid intake prevented continuous exposure with the current simulator.

The altitude simulators functioned properly on the morning of the first treatment day, with respect to removing 100% of the expired CO_2 and providing the desired average O_2. All 12 active simulators continued to remove all the expired CO_2 throughout the duration of the treatment period, but they did not

continue to provide the design levels of inspired O_2. The average inspired O_2 concentration rose by noon the first day, and remained elevated for the remainder of the treatment period. This dramatically lowered the effective altitude produced by the simulators from 3960 m to 3200-3550 m (average 3370 $\pm$ 517), which clearly compromised the ability of the simulators to induce altitude acclimation. It is possible to induce significant altitude acclimation at 3475 m with 7 days' continuous residence (12), but there are no reports of acclimation with intermittent exposures to this (or any other) altitude. Therefore, there was no way to predict either the likelihood or degree of any acclimation which the treatment period might have induced.

The cause of the reduction in the altitude equivalent could not be determined from the experimental measurements. There is a single report in the literature in which an exercise device having the same principle of operation, but designed to produce altitudes of only 1600-1700 m, was tested for its ability to maintain its inspired O_2 concentration (1). This device was found to produce higher inspired O_2 concentrations (lower effective altitude), as exercise intensity increased. Inspired O_2 was 17.12% at 40% VO_2 max, equivalent to 1670 m; 17.58% at 60% VO_2 max, equivalent to 1460 m; and 18.04% at 75% VO_2 max, equivalent to 1250 m; these are marked changes. Because increasing the exercise intensity increased ventilatory rate in that test, we suspect that a negative relationship exists between ventilatory rate and the inspired O_2 concentration of this type of device. Clearly, the <u>decreasing</u> O_2 concentration in the expired air, as exercise intensity increased, could not account for the <u>increasing</u> O_2 concentration in the inspired air. The increased ventilatory rate appears to be the only other possible mechanism.

Hypoxia stimulates ventilatory rate and markedly so (16). The experimental altitude simulators used in the current study initially induced a profound hypoxic stimulus equivalent to 3900 m, which, must have increased resting ventilation, although it was not measured. Such increased resting ventilation could have been the cause of the increased inspired O_2 concentration seen after the morning of the first day. We looked for just such a relationship between ventilatory rate and inspired O_2 concentration in the initial pilot tests of the device, but found only a slight, and apparently insignificant, tendency. The tests were relatively brief, however, as they consisted of progressive cycle ergometer exercise (3 min bouts, in 0.5 kp increments) to an exercise load that could not be sustained due to unacceptable heating of the inspired air by the exothermic CO_2 scrubber reaction. The highest exercise load tolerated by any subject was 2.5 kp, which required only 15 min to accomplish; most final loads were 2.0 kp, requiring 12 min. Such brief time intervals at the higher ventilatory rates may not have been long enough to permit the O_2 concentrations to increase to a detectable level. However, the 3-1/2 h morning session on the first treatment day was certainly long enough to both induce the hypoxic response (about 15-20 min) and allow the development of progressively higher inspired O_2 concentrations in response to the increasing, hypoxia-stimulated ventilatory rates. Such a situation would also provide negative feedback to limit the hypoxic stimulus: the higher ventilatory rates would reduce the level of hypoxia, which was stimulating the ventilation. If such negative feedback were occurring, a relatively stable equilibrium for the inspired O_2 concentrations would be seen at levels noticeably higher than the initial levels produced by the simulators. Higher

and relatively stable equilibrium concentrations were exactly what was observed throughout the course of the treatment period.

After the treatment period at sea level, the experimental group showed a significantly lower resting end-tidal PCO_2, indicating alveolar hyperventilation. The reduction in PCO_2 was accompanied by a significant reduction in RR of 16% and an increase of 13% in minute ventilatory rate. Together these represented a significant increase of 35% in calculated tidal volume, a large increase in depth of breathing. The corresponding change in the calculated tidal volume of the control group was a decrease of 26%, principally due to increased RR. The source of the increased tidal volume in the experimental group is not readily apparent. Because the experimental and control groups breathed through identical face masks and identical lengths of inspired and expired air tubing, the respiratory resistance must have been approximately equal for both groups. Neither group commented upon excessive respiratory resistance, so it is likely that any training of the ventilatory muscles over the ten-day period was probably slight and similar for both groups. It cannot be determined from our measurements when the experimental group developed their increased breathing depth, but we cannot exclude the possibility of a "carry-over" response from the experimental hypoxia for the short period while the ventilatory parameters were measured.

It was obvious from the ventilatory measurements that the experimental group had no ventilatory advantage upon ascent to 4500 m altitude. At altitude, both groups showed the expected increase in minute ventilation and decrease in end-tidal PO_2 and PCO_2 (4), with no significant differences between them. The minor differences existing initially between the groups at sea level

in PO_2 and PCO_2 were retained not only across the sea level treatment period but also after ascent. This indicated that, contrary to the original hypothesis, there were no major effects of simulator treatment upon ventilation during the altitude challenge. In fact, the increase in resting ventilatory rate seen on the first day after ascent to altitude in both groups was statistically significant only for the control group.

Acute altitude exposure results in hemoconcentration from extravasation of plasma water, while chronic altitude exposure results eventually in a true erythropoesis and an expansion of total blood volume (6,11). Both responses are beneficial, in that they result in an enhanced oxygen-transport capability per unit volume of blood, at least until the point that the increased blood viscosity interferes with the pressure-flow relationship (17). Pre-acclimation to altitude might also induce hemoconcentration, but this study's results indicated that simulator use at sea level did not induce such a response. In fact, PV, RCV, and total blood volume actually increased slightly in both groups, with the numerically greater increase in the control group. Upon ascent to altitude, both groups showed the expected hemoconcentration, and to a similar degree. This indicates that the lesser degree of hemodilution of the experimental group at sea level did not affect the ability to hemoconcentrate later at altitude.

Proof of acclimation, of course, was to be found in the AMS experience at altitude, not in any intervening ventilatory or hematological variables. In that regard, there were no significant differences in incidence of AMS between the experimental and control groups in either the global sickness experience or in the AMS-C and AMS-R scores calculated from the individual symptoms of the

ESQ. When just those who became ill were considered, the severity scores of the experimental and control groups were nearly identical. This is not to say that the experimental group may have received no benefit at all from the sea level treatment, however. The incidence of AMS, however measured, was always less in the experimental group than in the control group. For AMS-C, the difference approached, but did not reach, significance. Furthermore, the incidence of AMS-C and AMS-R in the experimental group appears to have been lower than that usually observed in untreated subjects exposed at 4570 m for 48 h in our hypobaric chamber. In a pooled sample of 25 different subjects at the identical altitude for 48 h(2), the incidence of AMS-C was 88% (95% confidence interval 75-100%) while that of AMS-R was 84% (95% confidence interval 69-99%). The control group in the present study had AMS-C incidence of 100% and AMS-R incidence of 80%, which were within the confidence intervals. The experimental group, however, had AMS-C incidence of 58% and AMS-R incidence of 50%. These both lay outside their respective confidence intervals and suggest that a slight degree of altitude pre-acclimation may have occurred in the experimental group, despite the lack of any significant difference from the control group.

It thus appears that the experimental altitude simulators were, at most, of only marginal benefit in reducing AMS symptomatology under the 7.5-h per day, 10-day treatment regimen used. Further, the devices failed to induce any ventilatory or hematological pre-acclimation. This was most disappointing, as anecdotal information (unpublished) from a number of trials by personnel of this laboratory have shown that 3-4 days exposure of 4,5 or 6 h duration at 4300 m on Pikes Peak will enable most individuals to remain there anywhere from 16 to 48 h without developing severe symptoms of AMS (moderate headache excluded).

The current study cannot rule out the possibility that a longer or more intense acclimating stimulus might have better effect. Designing a longer acclimating regimen appears to present a number of obstacles, however. It is difficult to envision any treatment regimen which eliminates the scheduled breaks to provide a more continuous stimulus. It is similarly difficult to see how exposures during the acclimating period could be extended, either in duration or number. Ten consecutive days of relative inactivity for a major portion of one's waking hours would appear to be the maximum period that possibly could be devoted to acclimation immediately before an ascent. The only feasible way to increase the acclimating stimulus appears to be redesigning the altitude simulator to tightly maintain an altitude equivalent in the 3960-4300 m range, despite the anticipated hypoxic ventilatory response. Even then, it is likely that any feasible treatment regimen would result in only partial pre-acclimation at best. Staging at appropriate altitudes during the ascent still appears to be the technique of choice to minimize the incidence and severity of AMS.

Acknowledgements

The authors wish to express their gratitude to James A. Devine, Joseph F. Gardella, David D. Hart and Edward A. Powers for their technical assistance and to the many soldiers from Ft. Bliss, TX and Ft. Devens, MA who volunteered to serve as test subjects.

The views, opinions, and/or findings contained in this report are those of the authors and should not be construed as an official department of the Army position, policy, or decision, unless so designated by other official documentation.

Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

Reference to specific equipment, trade names and manufacturers is for identification purposes only and does not imply indorsement by the U.S. Army or the U.S. Department of Defense.

References

1. Berryhill RA, Williams KR. Physiological responses to the PO_2 aerobic exerciser (Abstract). Sci. Med. Sports 1984; 16:123.

2. Burse RL, Rock PB, Fulco CS. Ability of cold pressor test to predict susceptibility to acute mountain sickness (Abstract). Fed. Proc. 1986; 45:884.

3. Carson RP, Evans WO, Shields JL. Symptomatology, pathophysiology and treatment of acute mountain sickness. Fed. Proc. 1969; 27:1085-91.

4. Dempsey JA, Forster HV. Mediation of ventilatory adaptations. Physiol. Rev. 1982; 62:262-346.

5. Dill DB, Costill DL. Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. J. Appl. Physiol. 1974; 37:247-8.

6. Dill DB, Horvath SM, Dahms TE, Parker RE, Lynch JR. Hemoconcentration at altitude. J. Appl. Physiol. 1969; 27:514-8.

7. Evans WO, Robinson SM, Horstman DH, Jackson RE, Weiskopf RB. Amelioration of the symptoms of acute mountain sickness by staging and acetazolamide. Aviat. Space Environ. Med. 1976; 47:512-6.

8. Forwand SA, Landowne M, Follansbee JN. Effect of acetazolamide on acute mountain sickness. New Eng. J. Med. 1968; 279:839-45.

9. Hackett PH. Mountain sickness: prevention, recognition, and treatment. Albany, CA: Mountain Travel, 1978.

10. Hackett PH, Rennie D, Levine HD. The incidence, importance, and prophylaxis of acute mountain sickness. Lancet 1976; ii:149-55.

11. Hannon JP, Vogel JA. Oxygen transport during early altitude acclimatization: a perspective study. Europ. J. Appl. Physiol. 1977; 36:285-97.

12. Hansen JE, Harris CW, Evans WO. Influence of elevation of origin, rate of ascent and a physical conditioning program on symptoms of acute mountain sickness. Mil. Med. 1967; 132:585-92.

13. Houston CS. High altitude illness. Disease with protean manifestations. J. A. M. A. 1976; 236:2193-5.

14. Johnson TS, Rock PB, Fulco CS, Trad LA, Spark RF, Maher JT. Prevention of acute mountain sickness by dexamethasone. N. Engl. J. Med. 1983; 310:683-6.

15. Int Civil Aviation Org. Manuel de l'atmosphere type OACI. Montreal: ICAO, 1954.

16. Lahiri S. Physiological responses and adaptations to high altitude. In: Robertshaw D, ed. Environmental Physiology II, Vol. 15. Baltimore: University Park Press, 1977: 217-51.

17. Levy MN, Share L. The influence of erythrocyte concentration upon the pressure-flow relationships in the dog's hind limb. Circ. Res. 1953; 1:247-55.

18. Rock PB, Johnson TS, Cymerman A, Burse RL, Falk LJ, Fulco CS. Effect of dexamethasone on symptoms of acute mountain sickness at Pikes Peak, Colorado (4300 m). Aviat. Space Environ. Med. 1987; 58: 668-72.

19. Sampson JB, Cymerman A, Burse RL, Maher JT, Rock PB. Procedures for the measurement of acute mountain sickness. Aviat. Space Environ. Med. 1983; 54:1063-73.

20. Sampson JB, Kobrick JL. The Environmental Symptoms Questionnaire: revisions and new field data. Aviat. Space Environ. Med. 1980; 51:872-7.

21. U.S. Government. United States patent 4,086,923: Altitude conditioning method and apparatus. Washington: U.S. Government Patent Office, May 2, 1978.

FIGURE LEGEND

Figure 1. Portable altitude simulator. Expired air from oronasal mask is ducted through left tube to fixed port above left mixing chamber, where portion is vented to atmosphere. Remainder is swirled with ambient air in mixing chambers on next inspiration and then drawn through CO_2 scrubber into right tube on succeeding inspirations. Direction of flow is controlled by one-way valves at base of tubes.

FIGURE 1

Table 1: Altitude equivalents (mean ± SD) of inspired P_{O2} during 10-day SL preacclimation of Experimental Group (n=12). Equivalents based on ICAO tables (15).

	Altitude Equivalent (m)		
Day	Morning (0730-0800)	Noon (1215-1245)	Afternoon (1545-1615)
1	3944 ± 460	3319 ± 616	3423 ± 649
2	3298 ± 533	2770 ± 984	3200 ± 558
3	3310 ± 515	3322 ± 509	3520 ± 692
4	3423 ± 350	3286 ± 509	3313 ± 332
5	3380 ± 396	3380 ± 521	3374 ± 555
6	3170 ± 491	3380 ± 549	3557 ± 521
7	3240 ± 475	3526 ± 405	3539 ± 482
8	3505 ± 405	3475 ± 387	3603 ± 369
9	3438 ± 326	3231 ± 500	3155 ± 631
10	3322 ± 266	3289 ± 597	(NOT DONE)
AVERAGE	3405 ± 430	3295 ± 579	3409 ± 546

Table 2: Resting ventilatory parameters (mean ± SE) before and after 10-days'preacclimation with simulators and after 1 and 2 days at 4572 m altitude. EXP = Experimental Group, CON = Control Group.

Parameter	Group	Pre-accl	Post-accl	Alt 1	Alt 2
$V_{E\ BTPS}$ (L/min)	EXP	14.6±2.1	16.5±1.5	18.6±1.9	16.5±0.4
	CON	16.3±1.8	14.3±1.1 ♯	16.4±1.2	17.7±1.4
RR (breath/min)	EXP	15.5±0.9 ⓪	13.0±1.2	14.5±1.0	14.8±1.6
	CON	12.6±1.8	14.9±0.9	17.1±1.6	15.3±1.2
$P_{O2\ ET}$ (torr)	EXP	121.4±3.3	121.6±3.1 ♯	55.9±2.5	56.6±3.8
	CON	116.0±2.8	113.9±2.7 ♯	51.4±2.2	53.8±2.8
$P_{CO2\ ET}$ (torr)	EXP	38.1±1.9 ⓪	34.0±1.8 ♯*	25.3±1.4	25.6±1.4
	CON	41.7±1.2	39.2±1.2 ♯	28.3±1.2	27.2±0.6

⓪: Pre-accl ≠ Post-accl, $p < 0.05$.

♯: Post-accl ≠ Alt 1, $p < 0.05$.

*: EXP ≠ CON, $p < 0.05$.

Table 3: Self-ratings for "feeling sick" (maximum experienced at any time during altitude exposure).

Rating	Assigned Value	EXP	CON
Not Sick	0	6 (50%)	3 (30%)
Slightly Sick	1	3 (25%)	2 (20%)
Mod. Sick	2	0	1 (10%)
Very Sick	3	3 (25%)	4 (40%)
Mean Score (all) ± SE		1.0±0.4	1.6±0.4
Mean Score (sick) ± SE		2.0±0.4	2.3±0.4

χ^2(sick-not sick) = 0.26, $0.5 < p < 0.9$

Table 4: Group means for peak levels of cerebral and respiratory forms of acute mountain sickness (AMS-C and AMS-R, respectively) during two-day altitude exposure.

	AMS-C		AMS-R	
SICK & WELL	EXP GP	CON GP	EXP GP	CON GP
Number	12	10	12	10
Mean Score	1.60	2.61	1.05	1.38
SE	0.43	0.38	0.18	0.22
t-score	1.64, df = 20		1.12, df = 20	
p-value	$0.1 < p < 0.2$		$0.2 < p < 0.3$	
SICK ONLY				
Number	7	10	6	8
Mean Score	2.83	2.61	1.54	1.60
SE	0.45	0.38	0.21	0.21
t-score	0.38, df = 15		0.25, df = 12	
p-value	$0.7 < p < 0.8$		$0.8 < p < 0.9$	
Sickness Incidence	58%	100%	50%	80%
χ^2 (sick-not sick)	3.27, df = 1		1.02, df = 1	
p-value	$0.05 < p < 0.1$		$0.1 < p < 0.5$	

Table 5: Hematologic changes with preacclimation at sea level and on the two mornings at altitude, calculated from hemoglobin concentration and hematocrit ratio by the method of Dill and Costill (4).

Parameter	Group	Sea level		Altitude	
		Pre-accl	Post-accl	Day 1	Day 2
Hemoglobin (mg/dl)	EXP	14.4±0.8	13.9±0.8	14.9±0.7**	15.4±1.0**
	CON	14.4±0.7**	13.2±0.8	14.3±0.7**	14.3±0.9**
Hematocrit (%)	EXP	48.0±2.6	48.3±2.3	50.8±2.9**	52.9±3.3**
	CON	47.9±3.4	47.0±3.0	48.3±2.7	49.1±3.8 *
Δ Blood vol (%)	EXP	+3.6	-6.7	-9.7	
	CON	+9.1	-7.7	-7.7	
Δ Red cell vol (%)	EXP	+4.5	-2.9	-1.1	
	CON	+7.0	-5.2	-3.6	
Δ Plasma vol (%)	EXP	+2.8	-10.3	-17.8	
	CON	+11.0	-9.9	-11.3	

*: different from Post-accl, $p < 0.05$

**: different from Post-accl, $p < 0.01$

END
DATE
FILMD
3-88
DTIC